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Short daily hemodialysis rapidly improves nutritional status in hemodialysis patients

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Short daily hemodialysis rapidly improves nutritional status in hemodialysis patients.

Background. Malnutrition is a common problem in maintenance hemodialysis patients and is associated with increased mortality and morbidity. Interventions such as oral or intravenous nutritional supplements have often failed to improve nutritional status. We studied the effect of a daily dialysis program on nutritional parameters.

Methods. Eight patients treated with standard hemodialysis (SHD) 4 to 5 hours three times per week were converted to daily hemodialysis (DHD) 2 to 2.5 hours six times per week. Serum albumin, prealbumin, and total cholesterol were evaluated every three months. Anthropometry and dietary evaluation were performed every six months.

Results. Serum albumin rose from 39.0 ± 2.6 to 42.0 ± 3.1 and 43.0 ± 2.6 g/L, prealbumin from 0.36 ± 0.04 to 0.41 ± 0.05 and 0.42 ± 0.1 g/L, total cholesterol from 1.7 ± 0.4 to 1.9 ± 0.4 and 1.8 ±0.3 g/L at baseline and at 6 and 12 months, respectively, after switching patients to DHD. Daily protein intake increased from 1.29 ± 0.20 g/kg/day to 1.48 ± 0.60 and 1.90 ± 0.70 ($P < 0.05$). These changes were accompanied by a dry body weight increase of 2.4 ± 1.6 kg ($P < 0.005$) at month 6 and 4.2 ± 2.8 kg at one year ($P < 0.05$). Lean body mass increased from 47.7 ± 4.9 kg to 49.1 ± 5.9 ($P < 0.05$) and 50.5 ± 6.2 ($P < 0.05$).

Conclusions. Daily hemodialysis appears to be a suitable method to improve nutritional status in maintenance dialysis patients.

Protein-energy malnutrition is a frequent complication in maintenance hemodialysis patients. In a recent French national cooperative study, the incidence of malnutrition ranged from 20 to 36% depending on the selection of nutritional parameters [1]. In addition, the association between malnutrition and morbidity and mortality has been well described [2, 3]. Strategies for preventing or treating malnutrition in chronic dialysis patients include an increase in the dialysis dose, oral dietary supplements, appetite stimulants, intradialytic parenteral nutrition, and potentially anabolic factors such as growth hormone or insulin-like growth factor-1 (IGF-1) [4]. However, these interventions may not always succeed at improving malnutrition.

Daily hemodialysis, defined as more than five sessions per week, is a more physiological method of treatment with fewer oscillations from normal physiologic parameters [5].

We report here a fairly good nutritional improvement in patients on daily hemodialysis.

Key words: malnutrition, chronic hemodialysis, diet and dialysis, maintenance dialysis, protein-energy.

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METHODS

Eight male patients aged 42.9 ± 14.4 years (range 21 to 66) undergoing standard hemodialysis (SHD) 4 to 5 hours three times per week for 9.5 ± 6.4 years (1 to 17), were converted to daily hemodialysis (DHD) 2 to 2.5 hours six times per week at the beginning of 1997. All patients had native arteriovenous fistulae. The etiology of renal failure was chronic glomerulonephritis ($N = 4$), interstitial nephritis ($N = 2$), nephroangiosclerosis ($N = 1$), and nephronophtisis ($N = 1$). All were anuric and were treated at home ($N = 3$) or in self-care dialysis units ($N = 5$).

Daily hemodialysis (DHD) indications were hypertension (patients 1, 2, 4, 5, and 7), inability to tolerate four- to five-hour sessions (anxiety or family problems, patients 3 and 5), inability to tolerate interdialytic interval (fluid overload, patients 6 and 7), and weight loss and malnutrition (patients 3 and 8).

For each patient, the total weekly time and the dialysis modalities were not changed between the two strategies. The only differences were the frequency and the duration of each session. The dialysis machines were Monitral SC, Hospal (Modella, Italy) ($N = 7$) and Fresenius 4008 B

(Fresenius Medical Care, Bad Homberg, Germany) ($N = 1$). The membranes used were polysulfone in six patients, poly-methylmetacrylate in one, and polymer caprin in the last one; the mean surface area was 1.6 ± 0.14 m^2 (1.3 to 1.8 m^2). Mean blood flow was 273 ± 30 mL/min (230 to 300 mL/min). Dialysate was bicarbonate buffered and the flow rate was 500 mL/min.

Patients did not receive specific advice for particular diet.

Predialysis and postdialysis plasma urea, potassium, calcium, and phosphorus levels were recorded weekly. Kt/V was calculated according to the Daugirdas second-generation formula [6]. C-reactive protein (CRP), serum albumin, prealbumin, and total cholesterol concentrations were measured every three months by standard methods.

The average daily intake of calories, protein, carbohydrate, fat and mineral were estimated every three months using four- to seven-day food records by the same dietician. Average daily ingestion of nutrients was calculated using computerized diet software (Bilnut 4; S.C.D.A. NUTRISOFT, Cerelles, France). Protein equivalent of nitrogen appearance (PNA) was measured by urea kinetic modeling according to Borah formulas using urea mass transfer [7]. Anthropometric measures were taken every three months (BMI and skinfold thicknesses). Fat free body mass (FFM) was calculated according to Durnin and Wormesley [8] and lean body mass (LBM) was deduced as body weight (BW) − FFM.

Because of the pilot nature of the study, there was no random allocation of DHD treatment and each patient served as his own control (that is, before − after study).

Data were collected before (baseline) and at 6 and 12 months after switching the patients to DHD.

Statistical analysis

All data were expressed as mean ± SD, and statistical analysis was performed by one way analysis of variance (ANOVA) for repeated measures (Statview 4; Abacus Concepts, Inc., Berkeley, CA, USA).

RESULTS

Nutritional parameters

Patients were under relative usual restricted diet during SHD period since they were all anuric. On DHD, they felt free from dietetic rules. Interdialytic weight gain per session decreased from 3.2 ± 1.1 to 1.7 ± 0.5 kg, but weekly interdialytic weight gain rose from 9.0 ± 2.2 kg on SHD to 11.3 ± 3.2 at six months ($P < 0.01$) and 11.5 ± 4.9 at one year ($P < 0.01$) of DHD. Daily protein intake increased significantly from 1.29 ± 0.20 g/kg/day on SHD to 1.48 ± 0.60 g/kg/day at six months and 1.9 ± 0.7 at one year of DHD ($P < 0.05$). There was no significant trend for an increase in energy intake (36.2 ± 10.2 kcal/kg/day at baseline, 41.2 ± 11.8 at six months, and 42.3 ± 13.4 at one year, P = NS; Table 1). PNA increased from 1.1 ± 0.2 g/kg/day at baseline to 1.3 ± 0.3 at six months and 1.4 ± 0.2 g/kg/day at one year.

Table 1. Daily nutrient and mineral intake before, at six months and one year after starting daily hemodialysis (DHD) program

	Baseline	6 month DHD	One year DHD
Protein *g/kg/day*	1.29 ± 0.29	1.48 ± 0.55	1.87 ± 0.66[a]
Energy *kcal/kg/day*	36.2 ± 10.2	41.2 ± 11.8	42.3 ± 13.4
Carbohydrate *g/kg/day*	227 ± 49	283 ± 57	281 ± 22[b]
Lipid *g/kg/day*	74 ± 23	90 ± 28	105 ± 32[a]
Calcium *mg/day*	515 ± 114	613 ± 293	829 ± 301
Phosphorus *mg/day*	983 ± 231	1135 ± 306	1329 ± 285[a]
Sodium *mg/day*	2174 ± 1033	2391 ± 646	3296 ± 1547
Potassium *mg/day*	2196 ± 621	2677 ± 846	2759 ± 645

[a] $P < 0.05$, [b] $P < 0.01$ (ANOVA, repeated measures)

Biochemical indicators of nutrition significantly increased as early as the third month after starting DHD (Figs. 1 and 2), as compared with the year before starting DHD. Mean serum albumin increased from 39.0 ± 2.6 to 43.0 ± 2.6 g/L ($P < 0.01$), prealbumin from 0.36 ± 0.04 to 0.42 ± 0.10 g/L ($P < 0.05$) and total cholesterol from 1.7 ± 0.4 to 1.8 ± 0.3 g/L ($P < 0.01$). Serum bicarbonate was 22.0 ± 2.8 mmol/L on SHD versus 23.0 ± 2.3 (P = NS) and 24 ± 3.7 mmol/L (P = NS) at six months and one year of DHD, respectively.

These changes were accompanied by an increase in dry body weight of 2.4 ± 1.6 kg at six months ($P < 0.005$) and 4.2 ± 2.8 kg at one year ($P < 0.05$; Fig. 3). BMI increased from 20.4 ± 2.3 kg/m^2 at baseline to 21.2 ± 2.3 ($P < 0.01$), 21.7 ± 2.1 ($P < 0.05$) at six months and one year, respectively, after switching to DHD. Lean body mass increased from 47.7 ± 4.9 kg to 49.1 ± 5.9 ($P < 0.05$) and 50.5 ± 6.2 ($P < 0.05$) as well as fat free body mass from 9.7 ± 4.9 to 10.7 ± 4.9 (P = NS) and 11.1 ± 5.3 kg ($P < 0.05$) at six and twelve months, respectively (Fig. 3).

All these improvements appear after some weeks of DHD [9] as shown in Figures 1 to 3.

Serum CRP was always lower than 5 mg/L, confirming the absence of chronic or acute inflammation at the time of measurement.

Cardiovascular and other observed changes

Tolerance of DHD sessions was excellent using a daily two-needle puncture of the arteriovenous fistula, without complications for any patient. During SHD, four of five hypertensive patients received antihypertensive medications (β blockers and angiotensin-converting enzyme inhibitors). Mean blood pressure (MBP) was normalized and antihypertensive medications were stopped in three of them within two months, the last patient being able to reduce his treatment by two thirds. MBP was 106.5 ± 16.2 mm Hg at baseline, 92.9 ± 13.0 mm Hg, and 96.5 ±

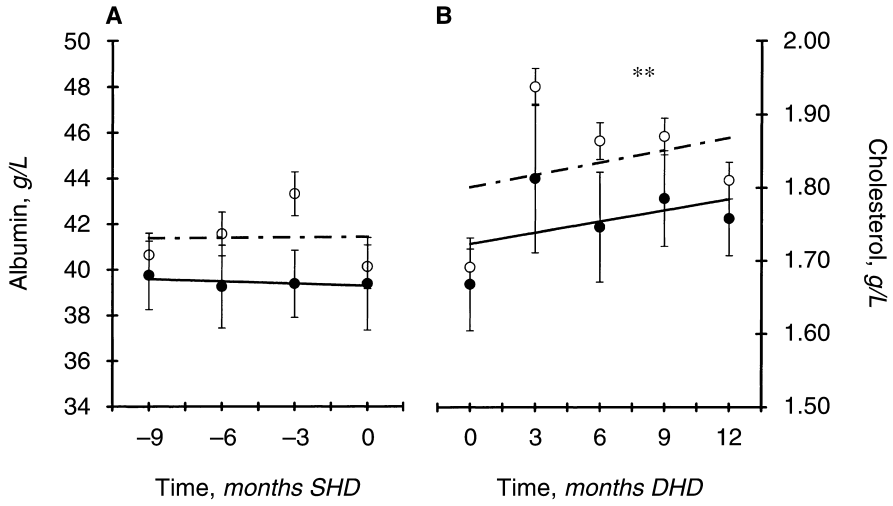

Fig. 1. Serum albumin (●) and total cholesterol (○) values before (SHD) (*A*) and after starting DHD (*B*). $^{**}P < 0.001$ from baseline (ANOVA repeated measures). The solid line represents the regression model for albumin variation over time, dashed line for cholesterol.

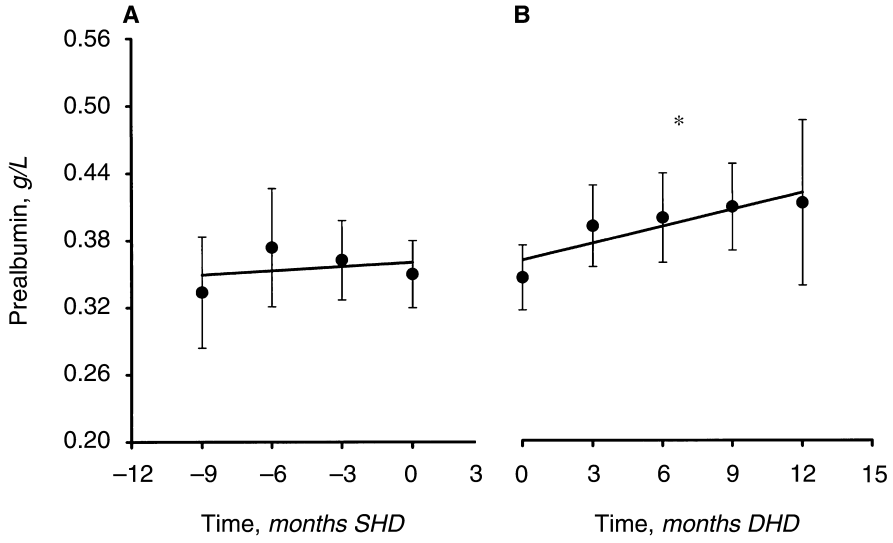

Fig. 2. Serum prealbumin values before (SHD) (*A*) and after starting daily hemodialysis (DHD) (*B*). $^{*}P < 0.05$ from baseline (ANOVA repeated measures). The solid line represents the regression model for prealbumin variation over time.

12.4 mm Hg at six months and one year of DHD, respectively. A reduction of left ventricular hypertrophy (LVH) measured by echocardiography 20- to 24-hours postdialysis session also was noticed. The left ventricular mass index calculated from Penn convention [10] decreased from 174 ± 53 g/m^2 at baseline to 146 ± 46 g/m^2 at six months and 134 ± 36 g/m^2 at one year ($P < 0.05$). There was no significant changes in the hemoglobulin (Hb) level in both strategies: 121 ± 28 versus 124 ± 29 g/L (P = NS), but we were able to reduce the dose of recombinant human erythropoietin (EPO) by 63%, from 3625 ± 3777 to 1375 ± 1407 U/patient/week ($P < 0.01$).

Predialysis urea concentration decreased by 23% from 30 ± 5.6 mmol/L to 23.2 ± 4.8 mmol/L on DHD. Urea time-averaged concentration (TAC) decreased from 19.9 ± 3.8 to 14.7 ± 3.3 mmol/L, and urea time averaged deviation (TAD) from 4.8 ± 1.1 mmol/L at baseline to 2.5 ± 0.6 mmol/L after switching to DHD [11]. The weekly Kt/V (w Kt/V) rose from 4.1 ± 0.4 to 4.5 ± 0.2 ($P < 0.01$).

We were also able to reduce Kayexalate by 66%, and phosphate binders (calcium bicarbonate and for one patient aluminum hydroxide) by 75% without further impairment in serum levels of potassium and phosphorus, despite a strong increase in phosphorus intake (Table 1), in favor of an increased clearance of these metabolites. Pre-dialysis phosphate on SHD was 2.22 ± 0.63 versus 1.83 ± 0.36 mmol/L at one year on DHD ($P < 0.05$).

DISCUSSION

This study shows that an increase in the frequency of dialysis sessions is associated with a strong and sustained

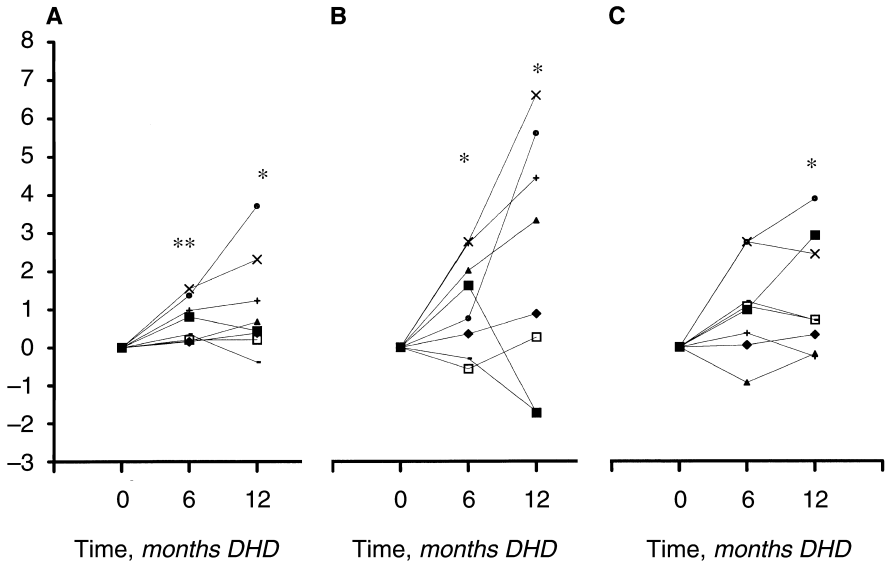

Fig. 3. Absolute intraindividual changes in body composition from baseline and during DHD as assessed by anthropometry. $^*P < 0.05$ from baseline (ANOVA repeated measures). (*A*) BMI, body mass index; (*B*) LBM, lean body mass; (*C*) FFM, fat free mass.

improvement in body composition in eight maintenance dialysis adult patients. We believe that this dialysis strategy is responsible for a dramatic increase in appetite and food intake of patients, thus rapidly improving nutritional status. Although the number of patients in this study is limited and there is some heterogeneity among etiology of renal disease and duration of maintenance dialysis, it should be noticed that each patient served as his own control, which gives acceptable baseline values for assessing the effects of DHD.

Our patients did not present malnutrition according to the recent nutrition DOQI guidelines [12], and they were not selected in this study for this purpose. Five of eight patients had a serum albumin level between 35 and 40 g/L, and no albumin was lower than 35 g/L; one patient had a serum prealbumin lower than 0.3 g/L. The patients' daily protein intake was greater than 1.2 g/kg in four and lower than 1 g/kg in one. Five patients had an energy intake lower than 35 kcal/kg, and for one of these five patients, energy intake was lower than 30 kcal/kg.

The nutritional status of these patients was close to the French national cooperative study that reported a mean serum albumin of 38.8 g/L, prealbumin of 0.34 g/L, and a nPNA of 1.13 g/kg/day [1]. Indeed, the average for our patients were 39.0 ± 2.6 g/L, 0.36 ± 0.04 g/L, and 1.1 ± 0.2 g/kg/day, respectively.

An improvement in the nutritional status also was found by other groups who routinely perform DHD. In a cohort study of 72 patients treated in nine centers between 1972 and 1996, Woods et al reported that the serum albumin rose by 2.9 g/L between month one and month twelve of treatment with DHD [13]; dry weight also increased at a rate of 0.85 kg per six months for one year.

Increasing frequency is more important than increasing dialysis dose [14]. Our patients had an adequate dialysis dose during SHD with a Kt/V per session of 1.4. When they were switched to DHD, the weekly Kt/V increased by 10% without increasing total dialysis time [15]. This is mainly due to a greater urea clearance during the first two hours of each dialysis session, thus increasing the K value of the Kt/V [16]. There is a correlation between the dose of dialysis and the protein intake estimated by nPNA [17], but this correlation is weak in stable hemodialysis patients (abstract; Kloppenburg et al, *J Am Soc Nephrol* 90:215, 1998). The clinical improvements on DHD are observed independently of important changes in Kt/V and thus, the benefits of increased frequency exceed what might be attributed to the modest gain in Kt/V [18].

How does DHD improve nutritional status? The main factor is an improved appetite reported in all patients and documented by the dietary interviews (Table 1). This may be due to a general well being, minor postdialysis fatigue, fewer dietetic rules, diminution in unpalatable medications, reduction of urea retention with less urea TAC, reduction in fluid overload with an interdialytic weight gain decrease from 3.2 ± 1.1 kg at baseline to 1.6 ± 0.5 kg with DHD, and a better homeostasis with 47% reduction of urea TAD.

Anorexia often starts before end-stage renal disease, as pointed out by Kopple et al [19] and Ikizler et al [20]. Indeed, these investigators have shown that when the GFR dropped under 20 mL/min, CRF patients spontaneously reduced their protein intake toward 0.9 g/kg/day and energy intake towards 26 kcal/kg/day [19]. After starting maintenance hemodialysis, these reduced intakes may be difficult to improve, despite intensive dietetic counseling. It is intriguing that in the present study,

patients dramatically increased their nutrient intakes despite increasing weekly Kt/V by only 10%. The free diet that includes free sodium and water intake and a disappearance of fear from fluid overload may partly explain these increased intakes. Alternatively, increased clearance of anorexic factors also may be present.

Other factors should be discussed, but are not yet proven: the diminution of protein metabolism disturbance due to a more physiological treatment, and a potential decrease in resistance to anabolic factors such as growth hormone, insulin, and insulin-like growth factor-1 (IGF-1). Improvement in leptin metabolism may have occurred, but we did not measure it at the time of this study.

Potential limitations of DHD may be present such as the repetition of the dialysis session could lead to an increased loss of amino acids, glucose, phosphate, and vitamins. These depletions have been well described in patients on long nightly hemodialysis with very high weekly Kt/V [21]. In our study, the weekly time was unchanged, the weekly Kt/V had slightly increased, the membranes used were biocompatible, and the dialyzers were not reused. Daily punctures of the AVF with two needles was possible and accepted without difficulty.

Presently, six sessions per week are more expensive than three, with a doubling cost of disposable and transportation, but this should be balanced with the reduction of drug expenses, particularly with the 63% reduction in EPO, and finally a low hospitalization frequency [22]. In addition, improvement in quality of life also was observed, with a perception of general health being increased from 55 to 80% [22].

Finally, DHD should be compared with other supports for the prevention or treatment of malnutrition in dialysis patients. Oral protein and energy supplements lead to little or only modest benefit. Intradialytic parenteral nutrition (IDPN) shows little or no improvement in patients' nutritional status. IDPN coupled with recombinant growth hormone is promising but expensive. Enteral tube feeding is efficient, but has a certain degree of discomfort [23, 24]. Anabolic factors such as IGF-1 are promising but still under evaluation [25].

CONCLUSION

The routine management of maintenance dialysis patients should be designed to prevent malnutrition. Protein energy malnutrition is a common complication in standard thrice-weekly hemodialysis. The present study shows that daily hemodialysis improves important nutritional markers in a rapid and sustained way. In order to treat renal failure related malnutrition, increasing dialysis frequency seems to be more logical and more efficient than other nutritional interventions such as parenteral or enteral feeding. Well-designed comparative studies with other methods of nutritional management should therefore be performed.

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